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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/975,899	10/12/2001	Douglas J. Goetz	D6379	1164

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/975,899	GOETZ ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 07/22/04 is acknowledged.

Claim 6 is pending

Claims 6 drawn to a method of treating cancer, comprising administering particles of biodegradable polymer or PEGylated copolymers comprising antibodies that bind to ICAM-1 expressed on an endothelial cells of irradiated tissue under consideration in the instant application.

The following new ground of rejection is necessitated by the amendment filed 07/22/04

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

3. Claim 6 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Hallahan (US Patent NO: 6,159,443) in view of WO 98/53852 , the know fact disclosed in the specification on pages 4, lines 3-20 ; 5, lines 1-5; and 10, lines 12-20 Mastrobattista et al.,(Biochim. Biophys. Acta, 1999, 1419, 353-363) and newly cited Patel et al (FASEB 1998, Vol.12 pages 1447-1454)

Applicant's arguments, filed on 07/22/04 have been fully considered, but have not been found convincing.

Applicant asserts that: (i) Mastobattista et al only teaches targeting immunoliposomes to epithelial cells in vitro not in vivo; (ii) US Patent '443 only teaches of a selectively targeting tumors by delivering radiation to target and also disclosed microspheres or liposomes as bio-compatible particles, that is not a partical of biodegradable polymer or PEGylated copolymer as claimed in the amended claim 6; (iii) at best the combination of prior art would suggest or motivate one of ordinary skill in the art to administer an anti-ICAM-1 immunoliposome comprising an active agent to irradiated tumor tissue. That is not Applicant;s invention.

Applicants have traversed the primary and the secondary references pointing to the differences between the claims and the disclosure in each reference. Applicant is respectfully reminded that the rejection is under 35 USC103 and that unobviousness cannot be established by attacking the references individually when the rejection is based on the combination of the references. see In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981) See MPEP 2145. This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968).

Contrary to Applicants's assertion US Patent '443 teaches a method of treating cancer , the method comprising steps of exposing a target tissue or organ to the ionizing radiation and administering P-selectin antibody labeled delivery vehicle that carry active agent to the tumors (see entire document, Abstract , column 6, lines 5-30 and column 13, lines 24-30 in particular). US Patent '443 teaches radiation –induced increase in P-selectin in irradiated tumor and that the present invention contemplate the selective targeting of tumors by delivering radiation to target tumors and using a delivery vehicles which bind to P-selectin. The use of radiation to control cellular adhesion molecules is a unique approach to the treatment of tumors (see column 6, lines 5-15 in particular). US Patent '443 teaches that delivery vehicle is a biodegradable particles bearing antibodies that specifically bind to a P-selectin (column 7-8 in particular). Applicant's attention is drawn to column 7, lines 45-65 that specifically disclosed biodegradable particle such as microspheres or liposomes as delivery vehicles. It is noted that the specification as filed disclosed liposomes as the examples of biodegradable particle (see page 11 lines 3-20 in particular).

Applicant's argues that US Patent '443 does not teach that P-selectin in expressed on an endothelial cell of irradiated tissue. However, this functional limitation would be obvious result of the effects of the ionizing radiation on irradiated tissue or organ taught by US Patent '443 because both the prior art and the instant invention administer the same treatment i.e. exposing a target tissue or organ to the ionizing radiation. Moreover, the specification clearly disclosed that it was known at the time the invention was made that P-selectin translocated to the cell membrane of endothelial cells within 30 minutes post irradiation (see page 9, lines 3-10 in particular) . Therefore it would be obvious to one of ordinary skill in the art at the time the invention was made to conclude that P-selectin would be in endothelial cells in irradiated tumors.

The claimed invention differs from the reference teaching in that US Patent '443 does not teach a particle of biodegradable polymers or PEGylated copolymers comprising antibodies that binds to ICAM-1.

WO'852 teaches that exposure tissue to irradiation causes an increase in expression of several cell adhesion molecules including ELAM-1, E-selectin and ICAM-1, in endothelial cells (see entire document, page 2, lines 15-25 and page 3, lines 1-10 in particular).

The known fact disclosed in the specification on pages 4, lines 3-20 ; 5, lines 1-5; and 10, lines 12-20 teaches that it has been known for over 15 years that exposure of normal and diseased tissue to irradiation causes an increase leukocyte infiltration and that the key component of this process is the adhesion of leukocytes to the microvascular endothelium. In response to biochemical stimuli the endothelium become activated and increases its expression of receptors of several cellular adhesion molecule including E-selectin, P-selectin and ICAM-1.

Mastrobattista et al. teach biomolecular carrier, bearing anti ICAM-1 antibodies (see entire document, Abstract in particular). With regards to issue that Mastrobattista et al., target anti-ICAM-1 immunoliposomes *in vitro* not *in vivo*. It is noted that Mastrobattista et al. clearly stated that biomolecular carrier, bearing anti ICAM-1 antibodies can be effectively used to delivery drugs to the sites where the expression of ICAM-1 is increased (see Abstract in particular).

Patel et al., teaches a generation a particle of biodegradable polymer or PEGylated copolymer as a new type of drug carrier (see entire document, Abstract in particular). Patel et al., teaches that one of the advantage of using said particles is that they are not rapidly removed from the circulation (see page 1448 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of WO'852, Mastrobattista et al., , known fact disclosed in Specification on pages 4, 3-20 ; 5, lines 1-5; and 10, lines 12-20 and Patel et al., to those of US Patent ' 443 and substitute biomolecular carrier bearing antibodies to one cellular adhesion molecule i.e. P-selectin to another type of particle of biodegradable polymers or PEGylated copolymers carrier bearing antibodies to another cellular adhesion molecule i.e. ICAM-1, since the expression of any one of them would be enhanced in target tissue after irradiation, to obtain a claimed method of treating cancer, comprising the steps of irradiating a target tissue or organ and administering the biomolecular carrier bearing antibodies that specific to ICAM-1.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because it has been known for over 15 years that exposure of normal and diseased tissue to irradiation causes an increase leukocyte infiltration and that the key component of this process is the adhesion of leukocytes to the microvascular endothelium, as taught by the known fact disclosed in the specification on pages 4, lines 3-20 and exposure tissue to irradiation

causes an increase in expression of several cell adhesion molecules including ELAM-1, E-selectin and ICAM-1, in endothelial cells, as taught by the WO'852 and P-selectin labeled delivery vehicle was used to delivery drugs to target cancer tissue or organ where the expression of this cell adhesion molecule was increased by exposure said tissue or organ to irradiation, as taught by US Patent '433 and biomolecular carrier, bearing antibodies to another cell adhesion molecules ICAM-1 effectively used to delivery drugs to the sites where the expression of ICAM-1 is increase, as taught by Mastrobattista et al. In addition, using a particle of biodegradable polymer or PEGylated copolymer as a new type of drug carrier is more advantage because they are not rapidly removed from the circulation as taught by Patel et al.

With regard to the issue that liposomes as bio-compatible particles is not a partical of biodegradable polymer or PEGylated copolymer as claimed in the amended claim 6.

It is noted that Applicant himself acknowledge that biogedradable particles are only one kind of drug carrier. Other classes of carriers include liposomes and microbubbles are known in the art and can be adapted to target a specific cell or tissue (see Applicant's arguments, filed on 07/22/04, overlapping pages 9 and 10 in particular). Said statement supports the Examiner position that it would be obvious to a person of ordinary skill in the art at the time the invention was made to substitute one type of biomolecular carrier i.e. immunoliposomes comprising antibodies that binds to ICAM-1 with another type of biodegradable particles, i.e. particle of biodegradable polymers or PEGylated copolymers, as taught by Patel et al. As has been acknowledge by the Applicant , the combined prior art teaches a method of treating a cancer in an individual comprising irradiating a target tissue and administering an anti-ICAM-1 immunoliposome (see Applicant's arguments, filed on 07/22/04, page 10 in particular).

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

4. No claim is allowed.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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